REMARKS

This Reply is responsive to the Office Action dated May 12, 2009. Claims 49-77 were pending in the application at the time the Office Action was issued. Claims 68-77 are withdrawn as being directed to a non-elected invention and claims 49-67 are under examination. Claims 50-53, 60, and 64-67 have been cancelled. Claims 49, 54, 57, and 61 have been amended. Specifically, claim 49 has been amended to incorporate the limitations of previously pending claims 53 and 60, namely that the composition is formulated as a dry powder and comprises protective antigen. In addition, claim 49 has been amended to remove the limitation of a mucosal administration device. This embodiment is now claimed in new dependent claim 79. Claims 54 and 61 have been amended to depend from claim 49. Claim 57 has been amended to include CpG as a type of adjuvant. Support for this amendment can be found in the specification at paragraph [0168] and Table 19 on pages 59 and 60 of the specification. New claim 78 is directed to an embodiment of the invention in which the dry powder is reconstituted as a liquid prior to administration to a mucosal surface. Support for new claim 78 can be found in the specification at paragraph [097]. No prohibited new matter has been introduced by way of these amendments.

Upon entry of this amendment, claims 49, 54-59, 61-63, and 68-79 will be pending in the application with claims 49, 54-59, 61-63, 78 and 79 under examination. Entry of the amendments and remarks submitted herein are respectfully requested.

I. Priority

According to the Office Action, the provisional applications allegedly do not provide written description support for compositions comprising mucosal administration devices, dry powder formulations, and specific adjuvants (*e.g.*, signaling transducer receptor of LPS, agonists of toll-like receptors, and positively-charged polysaccharides). Accordingly, the Examiner has assigned the claimed invention an effective filing date of February 11, 2005, the filing date of instant application. Applicants respectfully disagree with Examiner.

With respect to dry powder formulations, both provisional applications disclose that the vaccine compositions of the invention can be formulated as dry powders. For instance, at paragraphs [078] and [079] of the specification of U.S. Provisional Application No. 60/544,130,

filed February 11, 2004, the disclosure provides that vaccine injection solutions of the invention can be prepared from sterile powders and that unit doses of the vaccine compositions can be in powder form. A similar description is provided at paragraphs [077] and [078] of the specification of U.S. Provisional Application No. 60/544,848, filed February 12, 2004. Thus, claims directed to dry powder formulations are entitled to a priority date of February 11, 2004.

II. Specification

The Examiner has objected to the specification because Tables 2 and 5 purportedly cannot be read due to certain numbers having been cut off. The specification has been amended to replace Tables 2 and 5 with enlarged versions so that the numbers can be clearly read. However, Applicant notes that the specification submitted on August 11, 2006 upon entry into the national stage contained enlarged versions of Tables 2 and 5 on pages 33 and 39 of the specification, respectively. No new matter has been submitted by replacement of these tables. Applicant respectfully requests that the objection to the specification be withdrawn.

III. Claim Objections

Claims 64-67 have been objected to on the grounds that they fail to further limit the subject matter of the claim from which they depend. Specifically, the Examiner alleges that these claims, which are directed to different types of immune response elicited by the composition, do not further limit the structure of the composition. Without agreeing with the Examiner's reasoning and solely to expedite prosecution, claims 64-67 have been cancelled. Thus, the objection to these claims is moot.

IV. Rejections under 35 U.S.C. §112, first paragraph

Claims 49-67 have been rejected under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the written description requirement. According to the Office Action at pages 4-7, the specification does not provide adequate description of immunogenic fragments and epitopes of anthrax antigens that can be used in the compositions of the present invention. Relying on several literature publications describing the difficulty in defining functional epitopes, the Examiner asserts that one of skill in the art cannot readily ascertain immunogenic fragments and epitopes of the disclosed antigens without empirical testing. With respect to

claims 60-63, the Examiner asserts the specification fails to adequately describe the claimed genus of dry powder formulations of the compositions. Applicant traverses the rejection.

With respect to the alleged lack of written description of immunogenic fragments and epitopes, Applicant notes that none of the currently pending claims recites immunogenic fragments or epitopes of anthrax antigens. In fact, in an effort to expedite prosecution, claim 49 has been amended to specify that the composition comprises protective antigen.

With regard to the Examiner's assertion that claims directed to dry powder formulations do not satisfy the written description requirement, Applicant submits that one of skill in the art reading the specification would recognize that the Applicant was in possession of such formulations as of the filing date of the application. The specification describes a working example in which a dry powder formulation was made containing specific components and amounts of such components for immunization of rabbits. See Example 5 on pages 49-53 of the application. Methods of making dry powder formulations of therapeutic proteins are known to those of skill in the pharmaceutical arts. The specification clearly describes which components are present in the composition of the invention and describes that these compositions may be formulated as dry powders. Applicant is not required to describe every possible dry powder formulation of the claimed compositions, especially when the methods of making such formulations are known to those of skill in the art. All that is required to satisfy the written description requirement is a description of the claimed invention in sufficient detail to convey to one skilled in the art that the inventor had possession of the claimed invention as of the application filing date (see MPEP 2163, Section I). Applicant submits that the written description requirement is met and that the rejection of the claims under 35 U.S.C. §112, first paragraph be withdrawn.

V. Rejections under 35 U.S.C. §102(a)

Claims 49-53, 57, 58, and 60-67 have been rejected under 35 U.S.C. §102(a) as being anticipated by a literature publication to Miksztra *et al.* (Journal of Infectious Diseases, Vol. 191: 278-288, January 15, 2005). Miksztra *et al.* allegedly disclose dry powder formulations of recombinant protective antigen, CpG, trehalose, and chitosan loaded into capsules for intranasal delivery with a device. Applicant respectfully traverses the rejection.

Miksztra *et al.* was published electronically December 15, 2004 after the priority date of the instant application. The Examiner determined that claims directed to dry powder formulations were entitled to a priority date of February 11, 2005, the filing date of the instant application, thus making Miksztra *et al.* available as prior art. As discussed above in Section I, Applicant submits that the currently pending claims are entitled to a priority date of February 11, 2004, and therefore Miksztra *et al.* is not prior art. In any case, Applicant submits herewith a declaration under 37 C.F.R. §1.131 demonstrating that the currently claimed invention was reduced to practice prior to December 15, 2004, the effective date of the Miksztra *et al.* reference. Specifically, Exhibits A-B accompanying the declaration under 37 C.F.R. §1.131 document the production of dry powder formulations and immunization of rabbits with such dry powder formulations before December 15, 2004. The powder formulations and experimental protocol described in the Exhibits is identical to Example 5 of the instant application. Therefore, Applicant has demonstrated that the subject matter of the claims was invented prior to December 15, 2004 and Miksztra *et al.* is not available as prior art. Accordingly, the rejection of the claims under 35 U.S.C. §102(a) should be withdrawn.

VI. Rejections under 35 U.S.C. §103(a)

Claims 49-57 and 60-67 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Publication No. 2006/0134143 to Schneerson. Schneerson allegedly discloses recombinant protective antigen conjugated to a PGA peptide for immunization against anthrax. According to the Office Action, Schneerson also discloses that adjuvants, such as MPL can be included in the compositions and the compositions can be formulated in a variety of forms such as fluid, gels, pastes, powders, microspheres, and films for direct application to a mucosal surface. In addition, Schneerson purportedly discloses that the compositions can be included in kits that optionally include dispensing means, such as spray applicators. The Examiner asserts that it would have been *prima facie* obvious to one of skill in the art to combine the recombinant protective antigen conjugated to PGA peptide with MPL and formulate the composition as a dry powder and administer to a mucosal surface as allegedly suggested by Schneerson. Applicant respectfully disagrees with the Examiner and traverses the rejection.

Claim 49 as amended is directed to a dry powder composition comprising protective antigen and a mucosal adjuvant. Schneerson teaches the use of PGA peptide, which in some

embodiments can be conjugated to protective antigen, and describes a laundry list of additives that can be added to compositions comprising the PGA peptides, including pH control agents, local anesthetics, isotonizing agents, adsorption inhibitors, solubility enhancing agents, stabilizers, reducing agents, and adjuvants. In addition, Schneerson lists a myriad of forms for delivering the compositions including fluid or viscous solutions, gels, pastes, powders, microspheres and films. There is no suggestion in Schneerson that would direct the skilled artisan to select out specific components, such as particular adjuvants, and formulate the composition as a dry powder form out of all the disclosed variables to arrive at the claimed invention. *See In re Baird*, 16 F.3d 380 (Fed. Cir. 1994) (reversing rejection of claims for obviousness where reference disclosed a vast number of variables and there was no suggestion in the reference guiding skilled artisan to select the particular components of the claimed invention).

Applicant has demonstrated that dry powder compositions comprising protective antigen and mucosal adjuvants exhibit superior properties as compared to similar liquid formulations. For instance, Example 5 in the application demonstrates that a dry powder formulation comprising protective antigen, some of which was conjugated to PGA, and MPL (formulation #D6) produced statistically significant serum responses at 8 weeks as compared to the same composition formulated as a liquid (formulation #L8). See last sentence of paragraph of [0149] and Figure 9B. In addition, this dry powder composition protected 100% of animals challenged with over 160 LD_{50} equivalents of anthrax. Thus, given the disclosure of Schneerson, a skilled artisan would not be motivated to formulate dry powder vaccines comprising protective antigen and a mucosal adjuvant over any other type of formulation suggested in Schneerson, such as liquid formulations, gels, pastes or microspheres. Furthermore, Applicant has demonstrated that the dry powder formulations of the claimed invention have superior properties. Therefore, the claimed invention is nonobvious over Schneerson and Applicant respectfully requests that the rejection of the claims under 35 U.S.C. §103(a) be withdrawn.

Claims 49-58 and 64-67 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Schneerson in view of a Sigma Chemical Catalog page advertising an emulsion of MPL and TDM. The alleged teachings of Schneerson are described above. The Examiner acknowledges that Schneerson does not suggest using two adjuvants in the vaccine compositions comprising PGA conjugates, but nevertheless concludes that it would have been

obvious to one of skill in the art to use the recombinant protective antigen conjugated to PGA as taught by Schneerson with the MPL and TDM emulsion because the MPL and TDM emulsion has been prepared in a manner to reduce the toxic side effects of the two adjuvants but retain the ability to potently stimulate the immune system. Applicant respectfully traverses the rejection.

Claim 49 has been amended to specify that the composition comprises protective antigen and at least one mucosal adjuvant and is formulated as a dry powder. As discussed above, Schneerson merely lists a multitude of potential additives that can be included in the compositions comprising PGA conjugates without providing any direction to one of skill in the art which combinations of additives to select. In fact, the Examiner has acknowledged that Schneerson doesn't teach or suggest the use of a combination of adjuvants in the compositions. The MPL and TDM solution described in the Sigma catalog is a stable oil-in-water emulsion that can be used as an alternative to water-in-oil emulsions. Schneerson does not disclose the use of any water-in-oil emulsions as adjuvants so one of skill in the art would not be motivated to substitute the MPL and TDM emulsion for any of the disclosed adjuvants in Schneerson. Furthermore, the claimed compositions are dry powder compositions. The adjuvant emulsion described in the Sigma Catalog is intended to be used as an emulsion in a liquid formulation as it is prepared as a stable oil-in-water emulsion to "reduce the undesirable side effects of toxicity and allergenicity." Thus, the skilled artisan would actually be deterred from using such an emulsion in a dry powder formulation. Therefore, the cited references do not render the claimed invention obvious and the rejection of the claims under 35 U.S.C. §103(a) should be withdrawn.

Claims 49-67 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Schneerson in view of an abstract by Alpar *et al.* As described above, Schneerson allegedly discloses compositions comprising recombinant protective antigen conjugated to a PGA peptide with suitable adjuvants, such as MPL, and such compositions can be formulated in a variety of forms such as fluid, gels, pastes, powders, microspheres, and films for direct application to a mucosal surface. Schneerson does not disclose any combination of two adjuvants in the compositions. According to the Office Action, Alpar *et al.* disclose effective mucosal adjuvants, such as MPL, and that chitosan can enhance the effects of other adjuvants when administered intranasally. The Examiner asserts that it would have been obvious to one of skill in the art to formulate the PGA conjugated protective antigen taught by Schneerson with MPL and chitosan as taught by Alpar *et al.* for intranasal administration. Applicant traverses the rejection.

As detailed extensively above, Schneerson does not provide any direction to the skilled artisan on how to select among the large number of additives and types of formulations disclosed in the application. Furthermore, as acknowledged by the Examiner, Schneerson does not disclose or suggest any combination of mucosal adjuvants let alone a combination of MPL and chitosan. Alpar *et al.* does not make up for the deficiency in Schneerson. Alpar *et al.* does not teach or suggest a combination of MPL and chitosan. Alpar *et al.* merely list a number of adjuvants, including MPL, that have been shown to be effective mucosal adjuvants. In a separate context, Aplar *et al.* state that they have previously shown that chitosan can enhance the effects of other adjuvants and then go on to describe their experiments utilizing chitosan and Quil-A or cholera toxin-B subunit. The claimed invention is directed to dry powder formulations of protective antigen and at least one mucosal adjuvant. Neither Schneerson nor Alpar *et al.* teaches or suggests such dry powder anthrax antigen compositions. Moreover, as discussed above, Applicant has shown that the claimed dry powder compositions exhibit superior properties as compared to liquid formulations containing the same components. Thus, the claimed invention is nonobvious over Schneerson in view of Alpar *et al.* Applicant respectfully requests that the rejection of the claims under 35 U.S.C. §103(a) should be withdrawn.

CONCLUSION

This reply is fully responsive to the Office Action dated May 12, 2009. Applicant respectfully requests favorable reconsideration and allowance of the pending claims in view of the foregoing amendments and remarks.

Except for issue fees payable under 37 CFR §1.18, the commissioner is hereby authorized by this paper to charge any additional fees during the pendency of this application including fees due under 37 CFR §1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-1283. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 CFR §1.136(a)(3).

If the Examiner has any further questions relating to this Reply or to the application in general, she is respectfully requested to contact the undersigned by telephone so that allowance of the present application may be expedited.

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Respectfully submitted,
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